AMENDMENTS TO THE SPECIFICATION

Applicants direct entry of the replacement Sequence Listing that is concurrently submitted herewith into the present application.

After paragraph [0001], add the following new section heading and paragraph.

INCORPORATION-BY-REFERENCE OF MATERIAL ELECTRONICALLY SUBMITTED

Incorporated by reference in its entirety herein is a computer-readable nucleotide/amino acid sequence listing submitted concurrently herewith and identified as follows: 98,552 bytes ASCII (Text) file named "ReplacementSequenceListing" created November 10, 2011.

Replace paragraph [0014] with:

In one embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of M^1X_nTPLGP (SEQ ID NO: 214) or $M^1B_oPZ_mX_nTPLGP$ (SEQ ID NO: 215). In this embodiment, the superscript, 1, denotes the first position of the amino acid sequence of the wild-type G-CSF sequence (SEQ ID NO: 143), the subscripts n, o, and m are integers selected from 0 to 3, and at least one of X and B is threonine or serine, and when more than one of X and B is threonine or serine, the identity of these moieties is independently selected. Also in this embodiment, Z is selected from glutamate, any uncharged amino acid or dipeptide combination including MQ, GQ, and MV. In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of MVTPLGP (SEQ ID NO: 1), MQTPLGP (SEQ ID NO: 2), MIATPLGP (SEQ ID NO: 3), MATPLGP (SEQ ID NO: 4), MPTQGAMPLGP (SEQ ID NO: 5), MVQTPLGP (SEQ ID NO: 6), MQSTPLGP (SEQ ID NO: 7), MGQTPLGP (SEQ ID NO: 8), MAPTSSSPLGP (SEQ ID NO: 9), and MAPTPLGPA (SEQ ID NO: 10).

Replace paragraph [0015] with:

In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of M^1TPXBO_rP (SEQ ID NO: 225). In this embodiment the superscript, 1, denotes the first position of the amino acid sequence of the wild-type G-CSF sequence (SEQ

ID NO: 143), and the subscript r is an integer selected from 0 to 3, and at least one of X, B and O is threonine or serine, and when more than one of X, B and O is threonine or serine, the identity of these moieties is independently selected. In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: MTPTLGP (~~SEQ ID NO:4~~ SEQ ID NO: 228), MTPTQLGP (SEQ ID NO: 11), MTPTSLGP (SEQ ID NO: 12), MTPTQGP (SEQ ID NO: 13), MTPTSSP (SEQ ID NO: 14), M^1TPQTP (SEQ ID NO: 15), M^1TPTGP (SEQ ID NO: 16), M^1TPLTP (SEQ ID NO: 17), M^1TPNTGP (SEQ ID NO: 18), MTPLGP (SEQ ID NO: 19), M^1TPVTP (SEQ ID NO: 20), M^1TPMVTP (SEQ ID NO: 21), and $MT^1P^2TQGL^3G^4P^5A^6S^7$ (SEQ ID NO: 22).

Replace paragraph [0016] with:

In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of $LGX^{53}B_oLGI$ (SEQ ID NO: 217), wherein the superscript denotes the position of the amino acid in the wild type G-CSF amino acid sequence, and X is histidine, serine, arginine, glutamic acid or tyrosine, and B is either threonine or serine, and o is an integer from 0 to 3. In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: LGHTLGI (SEQ ID NO: 23), LGSSLGI (SEQ ID NO: 24), LGYSLGI (SEQ ID NO: 25), LGESLGI (SEQ ID NO: 26), and LGSTLGI (SEQ ID NO: 27).

Replace paragraph [0017] with:

In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of $P^{129}Z_mJ_qO_rX_nPT$ (SEQ ID NO: 218) wherein the superscript denotes the position of the amino acid in the wild type G-CSF amino acid sequence, and Z, J, O and X are independently selected from threonine or serine, and m, q, r, and n are integers independently selected from 0 to 3. In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: P^{129}ATQPT (SEQ ID NO: 28), P^{129}TLGPT (SEQ ID NO: 29), P^{129}TQGPT (SEQ ID NO: 30), P129TSSPT (SEQ ID NO: 31), P^{129}TQGAPT (SEQ ID NO: 32), P^{129}NTGPT (SEQ ID NO: 33), PALQPTQT (SEQ ID NO: 34), P^{129}ALTPT (SEQ ID NO: 35), P^{129}MVTPT (SEQ ID NO: 36), P^{129}ASSTPT (SEQ ID NO: 37), P^{129}TTQP (SEQ ID NO: 38), P^{129}NTLP (SEQ

ID NO: 39), P^{129}TLQP (SEQ ID NO: 40), MAP^{129}ATQPTQGAM (SEQ ID NO: 41), and MP^{129}ATTQPTQGAM (SEQ ID NO: 42).

Replace paragraph [0018] with:

In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of $PZ_mU_sJ_qP^{61}O_rX_nB_oC$ (SEQ ID NO: 219) wherein the superscript denotes the position of the amino acid in the wild type G-CSF amino acid sequence, and at least one of Z, J, O, and U is selected from threonine or serine, and when more than one of Z, J, O and U is threonine or serine, each is independently selected, X and B are any uncharged amino acid or glutamate, and m, s, q, r, n, and o are integers independently selected from 0 to 3. In another embodiment the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: P^{61}TSSC (SEQ ID NO: 43), P^{61}TSSAC (SEQ ID NO: 44), $LGIPTAP^{61}$LSSC (SEQ ID NO: 45), $LGIPTQP^{61}$LSSC (SEQ ID NO: 46), $LGIPTQGP^{61}$LSSC (SEQ ID NO: 47), $LGIPQTP^{61}$LSSC (SEQ ID NO: 48), $LGIPTSP^{61}$LSSC (SEQ ID NO: 49), $LGIPTQP^{61}$LSSC (SEQ ID NO: 50), $LGTPWAP^{61}$LSSC (SEQ ID NO: 51), $LGTPFAP^{61}$LSSC (SEQ ID NO: 52), P^{61}FTP (SEQ ID NO: 53), and $SLGAP^{58}TAP^{61}$LSS (SEQ ID NO: 54).

Replace paragraph [0019] with:

In another embodiment the G-CSF polypeptide comprises a mutant peptide sequence with the formula of $Ø_aG_pJ_qO_rP^{175}X_nB_oZ_mU_sΨ_t$ (SEQ ID NO: 220) wherein the superscript denotes the position of the amino acid in SEQ ID NO: 143, and at least one of Z, U, O, J, G, Ø, B and X is threonine or serine and when more than one of Z, U, O, J, G, Ø, B and X are threonine or serine, they are independently selected. Ø is optionally R, and G is optionally H. The symbol Ψ represents any uncharged amino acid residue or glutamate, and a, p, q, r, n, o, m, s, and t are integers independently selected from 0 to 3. In another embodiment the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: $RHLAQTP^{175}$ (SEQ ID NO: 55), $RHLAGQTP^{175}$ (SEQ ID NO: 56), QP^{175}TQGAMP (SEQ ID NO: 57), $RHLAQTP^{175}$AM (SEQ ID NO: 58), QP^{175}TSSAP (SEQ ID NO: 59), QP^{175}TSSAP (SEQ ID NO: 60), QP^{175}TQGAMP (SEQ ID NO: 61), QP^{175}TQGAM (SEQ ID NO: 62), QP^{175}TQGA (SEQ ID NO: 63), QP^{175}TVM (SEQ ID NO: 64), QP^{175}NTGP (SEQ ID NO: 65), and QP^{175}QTLP (SEQ ID NO: 66).

Replace paragraph [0022] with:

In one embodiment, the hGH polypeptide comprises a mutant peptide sequence with the formula of P^{133}JXBOZUK^{140}QTYS (SEQ ID NO: 221), wherein superscripts denote the position of the amino acid in (SEQ ID NO: 160); and J is selected from threonine and arginine; X is selected from alanine, glutamine, isoleucine, and threonine; B is selected from glycine, alanine, leucine, valine, asparagine, glutamine, and threonine; O is selected from tyrosine, serine, alanine, and threonine; and Z is selected from isoleucine and methionine; and U is selected from phenylalanine and proline. In another embodiment, the hGH polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: PTTGQIFK (SEQ ID NO: 72), PTTAQIFK (SEQ ID NO: 73), PTTLQIFK (SEQ ID NO: 74), PTTLYVFK (SEQ ID NO: 75), PTTVQIFK (SEQ ID NO: 76), PTTVSIFK (SEQ ID NO: 77), PTTNQIFK (SEQ ID NO: 78), PTTQQIFK (SEQ ID NO: 79), PTATQIFK (SEQ ID NO: 80), PTQGQIFK (SEQ ID NO: 81), PTQGAIFK (SEQ ID NO: 82), PTQGAMFK (SEQ ID NO: 83), PTIGQIFK (SEQ ID NO: 84), PTINQIFK (SEQ ID NO: 85), PTINTIFK (SEQ ID NO: 86), PTILQIFK (SEQ ID NO: 87), PTIVQIFK (SEQ ID NO: 88), PTIQQIFK (SEQ ID NO: 89), PTIAQIFK (SEQ ID NO: 90), P^{133}TTTQIFK^{140}QTYS (SEQ ID NO: 91), and P^{133}TQGAMPK^{140}QTYS (SEQ ID NO: 92).

Replace paragraph [0023] with:

In another embodiment, the hGH polypeptide comprises a mutant peptide sequence with the formula of P^{133}RTGQIPTQBYS (SEQ ID NO: 222) wherein superscripts denote the position of the amino acid in SEQ ID NO: 160; and B is selected from alanine and threonine. In another embodiment, the hGH polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: PRTGQIPTQTYS (SEQ ID NO: 93) and PRTGQIPTQAYS (SEQ ID NO: 94).

Replace paragraph [0024] with:

In another embodiment, the hGH polypeptide comprises a mutant peptide sequence with the formula of L^{128}XTBOP^{133}UTG (SEQ ID NO: 223) wherein superscripts denote the position of the amino acid in ~~SEQ ID NO:20~~ SEQ ID NO: 160; and X is selected from glutamic acid, valine and alanine; B is selcted from glutamine, glutamic acid, and glycine; O

is selcted from serine and threonine; and U is selected from arginine, serine, alanine and leucine. In another embodiment, the hGH polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: LETQSP^{133}RTG (SEQ ID NO: 95), LETQSP^{133}STG (SEQ ID NO: 96), LETQSP^{133}ATG (SEQ ID NO: 97), LETQSP^{133}LTG (SEQ ID NO: 98), LETETP^{133}R (SEQ ID NO: 99), LETETP^{133}A (SEQ ID NO: 100), LVTQSP^{133}RTG (SEQ ID NO: 101), LVTETP^{133}RTG (SEQ ID NO: 102), LVTETP^{133}ATG (SEQ ID NO: 103), and LATGSP^{133}RTG (SEQ ID NO: 104).

Replace paragraph [0025] with:

In another embodiment the hGH polypeptide comprises a mutant peptide sequence with the formula of M^{1}BPTX$_n$Z$_m$OPLSRL (SEQ ID NO: 224) wherein the superscript 1, denotes the position of the amino acid in SEQ ID NO: 159; and B is selected from phenylalanine, valine and alanine or a combination thereof; X is selected from glutamate, valine and proline Z is threonine; O is selected from leucine and isoleucine; and when X is proline, Z is threonine; and wherein n and m are integers selected from 0 and 2. In another embodiment, the hGH polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: M^{1}FPTE IPLSRL (SEQ ID NO: 105), M^{1}FPTV LPLSRL (SEQ ID NO: 106), and M^{1}APTPTIPLSRL (SEQ ID NO: 107).

Replace paragraph [0519] with:

In the N-terminal mutants, the N-terminus of a wild-type G-CSF, M^{1}TPLGPA (SEQ ID NO: 181), is replaced with either M^{1}X$_n$TPLGPA (SEQ ID NO: 226) or M^{1}B$_o$PZ$_m$X$_n$TPLGPA (SEQ ID NO: 227). Wherein n, o and m are integers ~~sleeted~~ selected from 0 to 3, and at least one of X, B and O is Thr or Ser. When more than one of X, B and O is Thr or Ser, the identity of these moieties is independently selected. Where they appear, superscripts denote the position of the amino acid in the wild-type starting sequence.

Replace paragraph [0521] with:

In these mutants, the N-terminus of a wild-type GCSF, M^{1}TPLGP (SEQ ID NO: 190), is replaced with M^{1}TPX$_n$B$_o$O$_r$P (SEQ ID NO: 216). Wherein n, o and r are integers ~~sleeted~~ selected from 0 to 3, and at least one of X, B and O is Thr or Ser. When more than one of X,

B and O is Thr or Ser, the identity of these moieties is independently selected. Where they appear, superscripts denote the position of the amino acid in the wild-type starting sequence.

Replace paragraph [0523] with:

This mutation is made for the purpose of maintaining G-CSF activity. In these mutants, the amino acid sequence containing H^{53}, $LGH^{53}SLGI$ (SEQ ID NO: 191) is mutated to ~~$LGH^{53}B_0LGI$~~ $\underline{LGX^{53}B_0LGI}$ $\underline{(SEQ\ ID\ NO:\ 217)}$, where [[$\Theta$]] $\underline{X}$ is H, S, R, E or Y, and B is either Thr or Ser.

Replace paragraph [0525] with:

In this type of mutant, the amino acid sequence encompassing P^{129}, $P^{129}ALQPT$ (SEQ ID NO: 192), is mutated to $P^{129}Z_mJ_qO_rX_nPT$ $\underline{(SEQ\ ID\ NO:\ 218)}$, wherein Z, J, O and X are independently selected from Thr or Ser, and m, q, r, and n are integers ~~sleeted~~ $\underline{selected}$ from 0 to 3.

Replace paragraph [0527] with:

In this type of mutant, the amino acid sequence surrounding P^{61}, $LGIPWAP^{61}LSSC$ (SEQ ID NO: 213), is replaced with $PZ_mU_sJ_qP^{61}O_rX_nB_oC$ $\underline{(SEQ\ ID\ NO:\ 219)}$, wherein m, s, q, r, n, and o are integers ~~sleeted~~ $\underline{selected}$ from 0 to 3, and at least one of Z, J, O, X, B and U is selected as either Thr or Ser. When more than one of Z, J, O X, B and U is Thr or Ser, each is independently selected.

Replace paragraph [0529] with:

In this type of mutant, the amino acid sequence at the C-terminus of a wild-type G-CSF, $RHLAQP^{175}$ (SEQ ID NO: 193) is replaced with $\emptyset_aG_pJ_qO_rP^{175}X_nB_oZ_mU_s\Psi_t$ $\underline{(SEQ\ ID}$ $\underline{NO:\ 220)}$, wherein a, p, q, r, n, o, m, s, and t are integers ~~sleeted~~ $\underline{selected}$ from 0 to 3, and at least one of Z, U, O, J, G, $\emptyset$, B and X is Thr or Ser and when more than one of Z, U, O, J, G, $\emptyset$, B and X are Thr or Ser, they are independently selected. $\emptyset$ is optionally R, and G is optionally H. The symbol Ψ represents any uncharged amino acid residue or E (glutamate).